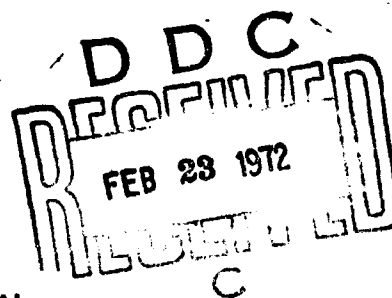


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THE EFFECTIVENESS OF BENACTYZINE HYDROCHLORIDE AND OTHER
ANTIMOTION SICKNESS DRUGS IN NEW COMBINATIONS

Charles D. Wood and Ashton Graybiel



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SUMMARY PAGE

THE PROBLEM

To compare the effectiveness of five different drug preparations in preventing motion sickness with that found for the combination of scopolamine 0.6 mg with d-amphetamine 10 mg in previous studies.

FINDINGS

Promethazine 25 mg plus d-amphetamine 10 mg was essentially equal to the baseline drug in range of effectiveness. Halving the doses of the baseline combination did not provide the protection it did in an earlier study. Benactyzine 3 mg was only slightly effective and when combined with d-amphetamine 10 mg was only moderately so. Promethazine 25 mg plus ephedrine 25 mg was about one-fourth less effective than the baseline preparation. The unexpected finding of the efficacy of small doses (25 mg) of promethazine plus ephedrine is pointed out, and the benefits from the relatively great reduction in side effects found with this drug combination are stressed.

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<p>Five different drug preparations are compared for their effectiveness in preventing motion sickness with the effectiveness found for the combination of scopolamine 0.6 mg with d-amphetamine 10 mg in previous studies. Promethazine 25 mg plus d-amphetamine 10 mg was essentially equal to the baseline drug in range of effectiveness. Halving the doses of the baseline combination did not provide the protection that it did in an earlier study. Benactyzine 3 mg was only slightly effective and when combined with d-amphetamine 10 mg was only moderately so. Promethazine 25 mg plus ephedrine 25 mg was about one-fourth less effective than the baseline preparation. The unexpected finding of the efficacy of small doses (25 mg) of promethazine plus ephedrine is pointed out, and the benefits from the relatively great reduction in side effects found with this drug combination are stressed.</p>		

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INTRODUCTION

In previous studies it was found that the combination of scopolamine hydrobromide with d-amphetamine sulfate was the most effective preparation for prevention of motion sickness, and this led to its being used as a "standard" for comparing the effectiveness of other drugs with parasympatholytic or sympathomimetic action. In this study we investigated the effectiveness of benactyzine hydrochloride and of combinations of other antinotion sickness drugs based on this standard.

PROCEDURE

The subjects were 10 healthy men, 18 to 21 years of age, who demonstrated normal responses in tests designed to measure the functional integrity of the otolithic and canalicular receptor systems of the inner ear. Each subject was rotated on a slow rotation room (SRR) and his susceptibility to motion sickness determined by means of the Dial Test (1). This test consists of setting the pointer on each of five dials arranged around the subject in such a manner as to require him to make five different head-body movements out of the plane of the room's rotation, generating the stressful accelerations. The head movements are paced by a tape recording that gives numbers to be set on the dials in randomized order at a rate of one every 6 seconds. The velocity (rpm) of the SRR at which severe malaise (M III) (2) was elicited during the execution of less than 50 head movements served as a subject's "control" susceptibility level. This speed of rotation was then maintained for that subject during subsequent experimental trials. Severe malaise, although a mild level of motion sickness, is of demonstrably high reliability as an endpoint under the circumstances of the present experiment.

Five different drug preparations, three of which were combined with others and one used alone, along with two placebos were administered according to a modified ten-unit Latin square design.

The drugs and placebos were placed in identical opaque gelatin capsules, and the double-blind technique of administration was used. A baseline was drawn by using the control and placebo values, and the change (increase) in number of head movements above the baseline was used to indicate the effectiveness of a drug or drug combination.

Drug Preparations:

scopolamine hydrobromide plus d-amphetamine sulfate	0.3 mg 5 mg
benactyzine hydrochloride	3 mg
benactyzine hydrochloride plus d-amphetamine sulfate	3 mg 10 mg
promethazine hydrochloride plus d-amphetamine sulfate	25 mg 10 mg
scopolamine hydrobromide plus d-amphetamine sulfate	0.6 mg 10 mg
promethazine hydrochloride plus ephedrine sulfate	25 mg 25 mg

RESULTS AND DISCUSSION

The results are summarized in Figure 1. The combination of scopolamine 0.6 mg with d-amphetamine 10 mg was (again) the most effective preparation tested. The increase in number of "tolerated" head movements with this combination of drugs was about the same as that reported previously, although the combination of scopolamine 0.3 mg with d-amphetamine 5 mg was found to be less effective than previously reported (3). Benactyzine in the 3-mg dose was only slightly effective under the conditions of this study. Moreover, in combination with d-amphetamine 10 mg it was only moderately effective, and it is doubtful, based on past experience with d-amphetamine (3), if the beneficial effects of the two drugs summated. Promethazine 25 mg combined with d-amphetamine 10 mg was found to be nearly as effective as when it was combined with scopolamine 0.6 mg, confirming earlier findings (4).

The unexpected finding was the efficacy of small doses (25 mg) of promethazine and ephedrine in combination. The 25 per cent reduction in effectiveness of that combination compared with the best combination, if confirmed, is more than compensated by the relatively great reduction in side effects. Moreover, this level of effectiveness is above that demonstrated (5) for many of the drugs used to prevent motion sickness under conditions of commercial travel, and repeated doses are not contraindicated.

RELATIVE EFFECTIVENESS OF ANTI-MOTION SICKNESS DRUGS

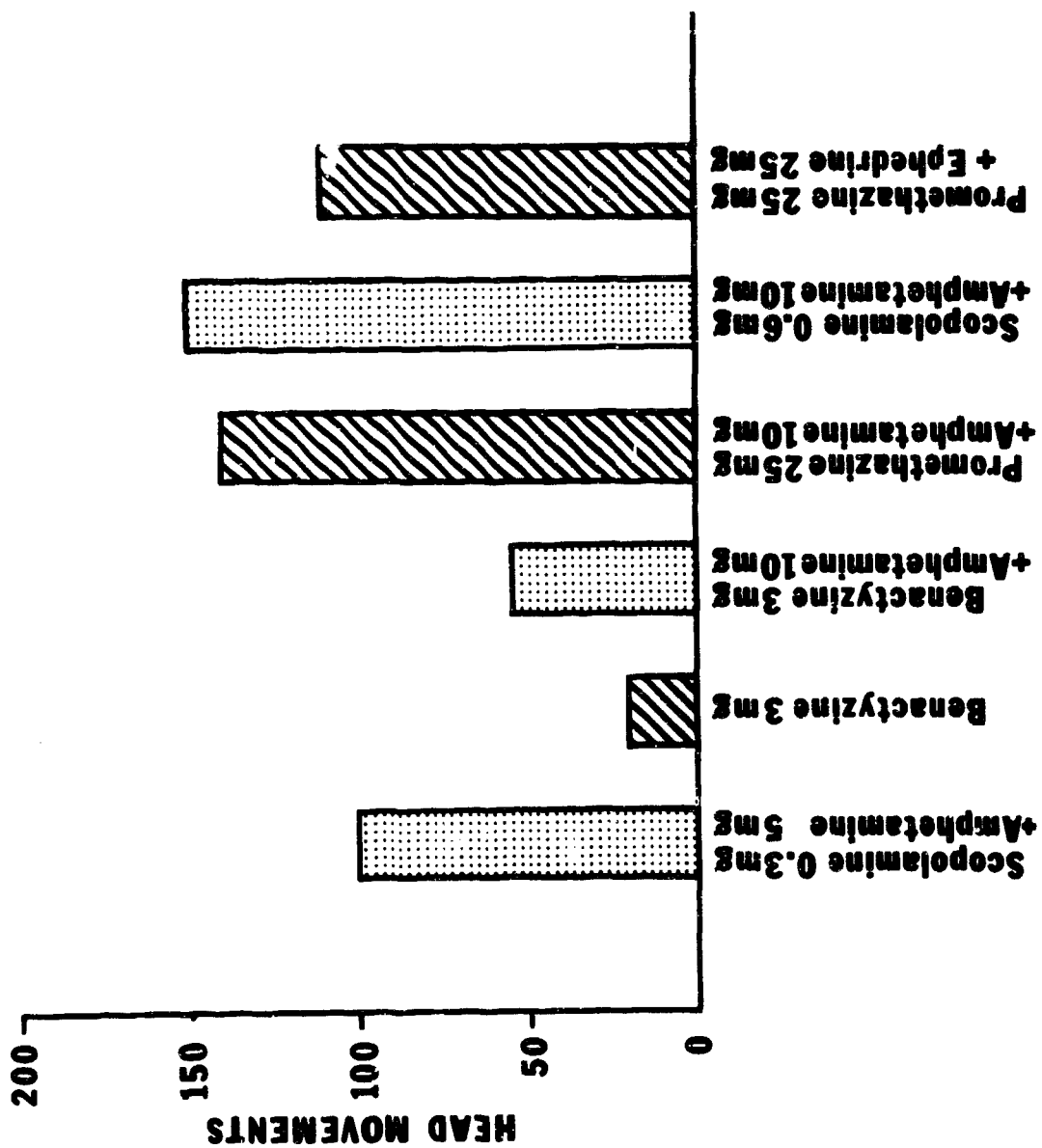


Figure 1
Effectiveness of each drug tested in terms of average increase above placebo level (zero line) in tolerated head movements.

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